

### **REMARKS/ARGUMENTS**

Claims 1-20 are pending in the captioned application. Claims 1-15 and 18-20 are under examination and are finally rejected. Claims 16 and 17 are hereby cancelled as they relate to a non-elected group of invention. Applicants reserve the right to prosecute these claims in one or more divisional applications. Applicants have also added new claim 21. Applicants respectfully request reconsideration and allowance of claims 1-15 and 18-21 in view of the following arguments.

Applicants first submit that claim 21 is added and depends on claim 12. Support for this new claim can be found in the specification, see page 10, line 32 through page 11, line 3; also see Example 4. Applicants submit that the claim is fairly based on the specification and no new matter is introduced.

Claims 1-15 and 18-20 are again rejected to as being unpatentable under 35 U.S.C. §103(a), over Wagner et al. (WO 2001/72458) in view of Bosman et al. (WO 1999/00670), Barner et al. (US 5986066), Badley et al. (US 6294391) and Nelson et al. (US 5955729). Applicants respectfully disagree.

Applicants have discussed Wagner et al. as well as the current invention in the previous response. Applicants also concluded that none of the other references provided suggested additional information which could be combined with Wagner et

al. to lead to the claimed invention. Nothing in the references teaches or suggests a method as claimed. A person skilled in the art would not have been able to come across the claimed invention without learning from the teaching of the specification.

In the Examiner's current rejection, the Examiner argues that Bosman et al. discuss the use of His-tag in immobilization of biomolecules. Specifically, the Examiner states that Bosman et al. discuss a method "wherein the presence of His-tags is exploited for covalent immobilisation of a biomolecule that contains said His-tag, and wherein the amino acid residues that comprise said His-tag are directly involved in the covalent bond".

In response, Applicants submit that there is a fundamental difference between the claimed invention and Bosman et al. In Bosman et al., the His-tag is not used in its conventional way (i.e. binding to a metal chelate) but as an agent for covalent immobilization and/or covalent conjugation of proteins/peptides to a support or carrier, see for example claim 1 of Bosman et al. Thus, in Bosman et al., the tag on the biomolecule has the primary function of forming a covalent bond with groups on the support. To increase the probability of this binding, the tag may have the further function of also binding to tag-binding compounds on the support. Thus, the tags are involved in both the covalent binding and the tag-specific binding.

In the present invention the solid support immobilization substrate is provided

with tag binding sites and activated reactive groups. Applicants have amended the claims to clearly state that the reactive groups “are capable of forming covalent bonds with the non-tag part of the biomolecules or biomolecules”. Applicants submit that this amendment is clearly supported by the specification, which teaches that the covalent coupling should be anywhere on the biomolecule but not on the tag. In the examples presented in the specification, the coupling is preferably done via activated carboxy acids. These give a stable amide binding with amines. In the case with the imidazol group in histidines, a labile coupling is obtained which is further reacted with amines which gives stable bonds or are hydrolyzed by water back to the acid. Therefore, it is implicitly taught that covalent coupling is not intended to the His-tag.

It is clear from the specification and the examples provided that the interaction of the biomolecules and the immobilization substrate includes both (1) the interaction of the tag on the biomolecule and the binding site for the tag from the immobilization substrate, as well as (2) the covalent bonding of the non-tag part of the biomolecules and the immobilization substrate. Applicants submit that this is neither taught or suggested by Bosman or any of the references. As such, Applicants submit that the claims are not rendered obvious by the references separately or combined.


Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of claims 1-15 and 18-21.

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Early and favorable consideration is respectfully requested.

Respectfully submitted,

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